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FILE COVERS 1907 - 19 Nov. 2002 VOL 137 ISS 21

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=> d all tot

L78 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:465749 HCAPLUS

DN 137:46052

TI Immunogenic cancer peptides: diagnosis and therapy

IN Calenoff, Emanuel; Ditlow, Charles C.

PA Northwestern University, USA

SO PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K

CC 15-2 (Immunochemistry)

Section cross-reference(s): 1, 8, 14

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047613	A2	20020620	WO 2001-US47734	20011113
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2002043314	A5	20020624	AU 2002-43314	20011113
PRAI	US 2000-723307	A	20001127		
	WO 2001-US47734	W	20011113		

AB The author discloses general methods and compns. that provide cancer-specific or highly cancer-assocd. antigens useful for diagnosis and treatment of cancer. The antigens are identified by their loss of

glycosylation on tumors vs. normal tissue with or without further modification (phosphorylation).

ST cancer antigen peptide diagnosis therapy

IT CD antigens  
 RL: PRP (Properties)  
 (CD66; identification of extracellular domain  
 -derived cancer-assocd. and cancer-  
 specific peptides)

IT Cadherins  
 RL: PRP (Properties)  
 (E-; identification of extracellular domain-derived  
 cancer-assocd. and cancer-specific peptides)

IT Immunoglobulins  
 RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST  
 (Analytical study); BIOL (Biological study); USES (Uses)  
 (G; to extracellular domain-derived peptides of  
 cancer-specific and cancer-assocd  
 . antigens)

IT Cadherins  
 RL: PRP (Properties)  
 (N-; identification of extracellular domain-derived  
 cancer-assocd. and cancer-specific peptides)

IT Imaging  
 (NMR; with proteins binding to extracellular domain  
 -derived peptides of cancer-specific and  
 cancer-assocd. antigens for)

IT Peptides, biological studies  
 RL: ANT (Analyte); ARG (Analytical reagent use); DGN (Diagnostic use); PRP  
 (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST  
 (Analytical study); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (asparagine-contg.; of extracellular domain of  
 cancer-specific and cancer-assocd  
 . antigens in relation to diagnosis and therapy)

IT Cell adhesion molecules  
 Proteins  
 RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST  
 (Analytical study); BIOL (Biological study); USES (Uses)  
 (binding to extracellular domain-derived peptides  
 of cancer-specific and cancer-  
 assocd. antigens by)

IT Diagnosis  
 (cancer; extracellular domain-derived  
 peptides of cancer antigens)

IT Peptides, biological studies  
 RL: ANT (Analyte); ARG (Analytical reagent use); DGN (Diagnostic use); PRP  
 (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST  
 (Analytical study); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (deglycosylated; of extracellular domain  
 of cancer-specific and cancer-  
 assocd. antigens in relation to diagnosis and  
 therapy)

IT Neoplasm  
 (diagnosis; extracellular domain-derived peptides  
 of cancer antigens)

IT Tumor markers  
 (extracellular domain-derived peptides of  
 cancer antigens)

IT Algorithm  
 (for identification of extracellular domain-derived  
 peptides of cancer antigens)

IT Immunoglobulins

RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(fragments; to **extracellular domain-derived peptides of cancer-specific and cancer-assocd. antigens**)

IT **Protein motifs**  
(glycosylation site; is absent for **extracellular domain-derived peptides of cancer-specific and cancer-assocd. antigens**)

IT CD40 (antigen)  
CD44 (antigen)  
Epidermal growth factor receptors  
neu (receptor)  
RL: PRP (Properties)  
(identification of **extracellular domain-derived cancer-assocd. and cancer-specific peptides**)

IT **Antibodies**  
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(monoclonal; to **extracellular domain-derived peptides of cancer-specific and cancer-assocd. antigens**)

IT **Prostate gland**  
(**neoplasm**; identification of **extracellular domain-derived cancer-assocd. and cancer-specific peptides**)

IT **Immunoassay**  
(of antibodies to **extracellular domain-derived peptides of cancer-specific and cancer-assocd. antigens**)

IT **Phosphopeptides**  
RL: ANT (Analyte); ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(of **extracellular domain of cancer-specific and cancer-assocd. antigens** in relation to diagnosis and therapy)

IT **Phosphorylation, biological**  
(protein; of **extracellular domain-derived peptides of cancer-specific and cancer-assocd. antigens**)

IT **Antitumor agents**  
(proteins binding to **extracellular domain-derived peptides of cancer-specific and cancer-assocd. antigens**)

IT **Carcinoma**  
(squamous cell; identification of **extracellular domain-derived cancer-assocd. and cancer-specific peptides**)

IT **Antibodies**  
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(to **extracellular domain-derived peptides of cancer-specific and cancer-assocd. antigens**)

IT **Antigens**  
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)  
(**tumor-assocd.**; identification and application of **extracellular domain-derived peptides of**)

IT **Antigens**

RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)  
 (tumor-specific antigens; identification  
 and application of extracellular domain-derived  
 peptides of)

IT Vaccines  
 (tumor; extracellular domain-derived  
 peptides of cancer-specific and cancer-  
 assocd. antigens)

IT Imaging  
 (tumor; proteins binding to extracellular  
 domain-derived peptides of cancer-specific  
 and cancer-assocd. antigens for)

IT Antitumor agents  
 (vaccines; extracellular domain-derived peptides of  
 cancer-specific and cancer-assocd  
 . antigens)

IT Integrins  
 RL: PRP (Properties)  
 (.alpha.v; identification of extracellular domain  
 -derived cancer-assocd. and cancer-specific  
 peptides)

IT Integrins  
 RL: PRP (Properties)  
 (.alpha.3; identification of extracellular domain  
 -derived cancer-assocd. and cancer-specific  
 peptides)

IT Transforming growth factor receptors  
 RL: PRP (Properties)  
 (.beta.-transforming growth factor type II; identification of  
 extracellular domain-derived cancer-assocd.  
 and cancer-specific peptides)

IT Integrins  
 RL: PRP (Properties)  
 (.beta.1; identification of extracellular domain  
 -derived cancer-assocd. and cancer-specific  
 peptides)

IT 437614-84-1 437614-85-2 437614-86-3 437614-87-4 437614-88-5  
 437614-89-6 437614-90-9 437614-91-0 437614-92-1 437614-93-2  
 437614-94-3 437614-95-4 437614-96-5 437614-97-6 437614-98-7  
 437614-99-8 437615-00-4 437615-01-5  
 RL: PRP (Properties)  
 (identification of extracellular domain-derived  
 cancer-assocd. and cancer-specific peptides)

IT 437975-00-3  
 RL: PRP (Properties)  
 (unclaimed sequence; immunogenic cancer peptides, diagnosis  
 and therapy)

L78 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:185159 HCAPLUS

DN 136:244041

TI A method for identifying peptide sequences having a specific functionality

IN Schneider, Gisbert; Eichler-Mertens, Mathias; Wrede, Paul

PA Callistogen A.-G., Germany

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-00

CC 9-16 (Biochemical Methods)

Section cross-reference(s): 1, 34

FAN.CNT 1

PATENT NO.

KIND DATE

APPLICATION NO. DATE

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 PI WO 2002020564 A2 20020314 WO 2001-EP10195 20010905  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,  
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
 US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 AU 2001093794 A5 20020322 AU 2001-93794 20010905  
 PRAI US 2000-655056 A 20000905  
 WO 2001-EP10195 W 20010905  
 AB The present invention relates to a method for creating a sequence-function  
 relationship, a method for identifying or generating peptide sequences  
 having a specific functionality, using the created sequence-function  
 relationship and a method for generating a focussed synthetic peptide  
 library. The PepHarvester algorithm was applied to the HSP70 binding  
 peptide LHIYTT. By using a diversity index of 0.1, 40 variants were  
 created.  
 ST peptide sequence specific function relationship; PepHarvester algorithm  
 HSP70 binding peptide variant creation  
 IT Histocompatibility antigens  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (HLA, class I; method for identifying peptide sequences having a  
 specific functionality)  
 IT Heat-shock **proteins**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (HSP 70, peptides binding to; method for identifying peptide sequences  
 having a specific functionality)  
 IT p53 (**protein**)  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (HSP70-binding peptides of; method for identifying peptide sequences  
 having a specific functionality)  
 IT **Proteins**  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (MART-1, MHC class I-binding tumor-specific peptide of, as seed  
 peptide; method for identifying peptide sequences having a specific  
 functionality)  
 IT Histocompatibility **antigens**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (MHC (major histocompatibility complex), class I, **tumor-**  
**specific** peptide of MART-1 binding to; method for identifying  
 peptide sequences having a specific functionality)  
 IT Histocompatibility antigens  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (MHC (major histocompatibility complex), peptides binding to; method  
 for identifying peptide sequences having a specific functionality)  
 IT Neoplasm  
 (MHC class I-binding tumor-specific peptides creation; method for  
 identifying peptide sequences having a specific functionality)  
 IT **Algorithm**  
 (PepHarvester; method for identifying peptide sequences having a  
 specific functionality)  
 IT Angiotensin receptor antagonists  
 (angiotensin II; method for identifying peptide sequences having a  
 specific functionality)  
 IT Vasopressin receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists or agonists; method for identifying peptide sequences

- having a specific functionality)
- IT **Protein motifs**
  - (cleavage sites; method for identifying peptide sequences having a specific functionality)
- IT T cell (lymphocyte)
  - (cytotoxic, peptide epitope sequences induction in human of; method for identifying peptide sequences having a specific functionality)
- IT Bioassay
  - (identified peptide sequences testing in; method for identifying peptide sequences having a specific functionality)
- IT Biological transport
  - Dopamine agonists
  - Dopamine antagonists
  - Drug design
  - Epitopes
  - Human
  - Hydrophilicity
  - Hydrophobicity
  - Peptide library**
  - Physical properties
  - Polarity
  - Protein sequences**
  - Refractive index
  - Statistical analysis**
  - Structure-activity relationship**
  - Surface area
  - Vaccines
  - Volume
    - (method for identifying peptide sequences having a specific functionality)
- IT Endothelin receptors
  - Hormone receptors
  - Neuropeptides
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (method for identifying peptide sequences having a specific functionality)
- IT **Peptides, biological studies**
  - RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (method for identifying peptide sequences having a specific functionality)
- IT **Amino acids, properties**
  - RL: PRP (Properties)
    - (method for identifying peptide sequences having a specific functionality)
- IT Evolution
  - (mol.; method for identifying peptide sequences having a specific functionality)
- IT **Simulation and Modeling, biological**
  - Simulation and Modeling, physicochemical**
    - (neural network; method for identifying peptide sequences having a specific functionality)
- IT **Proteins**
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (peptide inhibitors of assembly of; method for identifying peptide sequences having a specific functionality)
- IT Stability
  - (peptide; method for identifying peptide sequences having a specific functionality)
- IT G **protein-coupled receptors**
  - Heat-shock **proteins**
  - Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(peptides binding to; method for identifying peptide sequences having a  
specific functionality)

IT Human immunodeficiency virus  
(receptors, peptides binding to; method for identifying peptide  
sequences having a specific functionality)

IT **Molecular structure-property relationship**  
(stability, peptide; method for identifying peptide sequences having a  
specific functionality)

IT Immunization  
(vaccination; method for identifying peptide sequences having a  
specific functionality)

IT 403666-90-0 403666-91-1 403666-92-2 403666-93-3 403666-94-4  
403666-95-5 403666-96-6 403666-97-7 403666-98-8 403666-99-9  
403667-00-5 403667-01-6 403667-02-7 403667-03-8 403667-04-9  
403667-05-0 403667-06-1 403667-07-2 403667-08-3 403667-09-4  
403667-10-7 403667-11-8 403667-12-9 403667-13-0 403667-14-1  
403667-15-2 403667-16-3 403667-17-4 403667-18-5 403667-19-6  
403667-20-9 403667-21-0 403667-22-1 403667-23-2 403667-24-3  
403667-25-4 403667-26-5 403667-27-6 403667-28-7

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(amino acid sequence, PepHarvester algorithm-generated HSP70-binding  
peptide; method for identifying peptide sequences having a specific  
functionality)

IT 403666-69-3 403666-70-6 403666-71-7 403666-72-8 403666-73-9  
403666-74-0 403666-75-1 403666-76-2 403666-77-3 403666-78-4  
403666-79-5 403666-80-8 403666-81-9 403666-82-0 403666-83-1  
403666-84-2 403666-85-3 403666-86-4 403666-87-5 403666-88-6

RL: PRP (Properties)  
(amino acid sequence, PepHarvester algorithm-generated MHC class  
I-binding tumor-specific peptide; method for identifying peptide  
sequences having a specific functionality)

IT 403666-89-7  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(amino acid sequence, as HSP70-binding seed peptide; method for  
identifying peptide sequences having a specific functionality)

IT 156251-11-5  
RL: PRP (Properties)  
(amino acid sequence, as MHC class I-binding tumor-specific seed  
peptide; method for identifying peptide sequences having a specific  
functionality)

IT 156250-93-0 156251-12-6 156251-13-7 403667-29-8 403667-30-1  
403667-31-2 403667-32-3 403667-33-4

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(amino acid sequence, as calcd. HLA-0201 epitope of MART-1 protein;  
method for identifying peptide sequences having a specific  
functionality)

IT 220087-98-9 403667-34-5 403667-35-6 403667-36-7 403667-37-8  
403667-38-9 403667-39-0 403667-40-3 403667-41-4 403667-42-5  
403667-43-6 403667-44-7 403667-45-8 403667-46-9 403667-47-0  
403667-48-1 403667-49-2 403667-50-5 403667-51-6 403667-52-7  
403667-53-8 403667-54-9 403667-55-0 403667-56-1 403667-57-2  
403667-58-3 403667-59-4 403667-60-7

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(amino acid sequence, as calcd. HSP70-binding peptide in protein p53;  
method for identifying peptide sequences having a specific  
functionality)

IT 9015-82-1, ACE  
RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (inhibitors, peptides binding to; method for identifying peptide sequences having a specific functionality)
- IT 37259-58-8, Serine protease 37353-41-6, Cysteine protease 78169-47-8, Aspartylprotease 81669-70-7, Metalloprotease 158736-49-3, .b ta.-Secretase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; method for identifying peptide sequences having a specific functionality)
- IT 9001-92-7, Protease  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (prediction of cleavage sites for; method for identifying peptide sequences having a specific functionality)
- IT 267000-55-5 404012-83-5 404012-84-6 404012-85-7  
 RL: PRP (Properties) (unclaimed sequence; method for identifying peptide sequences having a specific functionality)
- L78 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS  
 AN 2002:52467 HCAPLUS  
 DN 136:245335  
 TI Dysadherin, a cancer-associated cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis  
 AU Ino, Yoshinori; Gotoh, Masahiro; Sakamoto, Michiie; Tsukagoshi, Kiyomi; Hirohashi, Setsuo  
 CS Pathology Division, National Cancer Center Research Institute, Tokyo, 104-0045, Japan  
 SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(1), 365-370  
 CODEN: PNASA6; ISSN: 0027-8424  
 PB National Academy of Sciences  
 DT Journal  
 LA English  
 CC 14-1 (Mammalian Pathological Biochemistry)  
 Section cross-reference(s): 3, 6, 13
- AB The authors report the cloning and characterization of a **cancer-assocd.** cell membrane glycoprotein recognized by mAb NCC-3G10. The antibody showed strong reactivity to a wide variety of cancer cells, but only to a limited no. of normal cells including lymphocytes, endothelial cells, and basal cells of stratified squamous epithelium. The cDNA for the **antigen** encodes 178 aa, which includes a putative signal sequence, a potential O-**glycosylated extracellular domain**, a single transmembrane domain, and a short cytoplasmic tail. Transfection of the cDNA into PLC/PRF/5 liver cancer cells resulted in reduced cell-cell adhesiveness, based on both morphol. and results of Ca<sup>2+</sup>-dependent cell aggregation assay. In transfected cells, E-cadherin was markedly decreased at the **protein** level in inverse proportion to the expression level of the **antigen** recognized by NCC-3G10, but not at the mRNA level. Aggregation of the **antigen** by NCC-3G10-coated beads triggered accumulation of actin, suggesting some interplay between this **antigen** and E-cadherin through actin. When metastatic ability was examd. in severe combined immunodeficient mice by injecting PLC/PRF/5 cells into the spleen, the transfectants formed a markedly higher no. of metastatic nodules in comparison with controls. The authors have named this cell membrane glycoprotein, which down-regulates E-cadherin and promotes metastasis, dysadherin.
- ST dysadherin cancer assocd plasma membrane E cadherin downregulation metastasis; sequence dysadherin cDNA human
- IT Cadherins  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study) (E-; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)



- IT Skin  
(basal cell; dysadherin, cancer-assocd. cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis in relation to expression in limited no. of normal cells)
- IT Cell membrane  
Human  
Liver, neoplasm  
Lung, neoplasm  
Neoplasm  
**Protein sequences**  
Stomach, neoplasm  
**cDNA sequences**  
(cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
- IT Cell adhesion  
**Protein motifs**  
Self-association  
(cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis in relation to)
- IT Actins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis in relation to)
- IT Cell aggregation  
(calcium-dependent; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis in relation to)
- IT Uterus, neoplasm  
(cervix; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
- IT Intestine, neoplasm  
(colon; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
- IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(dysad; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
- IT New natural products  
(dysadherin (protein))
- IT T cell (lymphocyte)  
(dysadherin, cancer-assocd. cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis in relation to expression in limited no. of normal cells)
- IT **Proteins**  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); NPO (Natural product occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)  
(dysadherin; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
- IT Blood vessel  
(endothelium; dysadherin, cancer-assocd. cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis in relation to expression in limited no. of normal cells)
- IT Neoplasm  
(metastasis; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
- IT Bladder  
Esophagus  
Mammary gland  
(neoplasm; cDNA sequence of dysadherin, cancer-assocd. cell membrane

- glycoprotein, that down-regulates E-cadherin and promotes metastasis)
- IT 7440-70-2, Calcium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(-dependent cell aggregation; cDNA sequence of dysadherin,  
cancer-assocd. cell membrane glycoprotein, that down-regulates  
E-cadherin and promotes metastasis in relation to)
- IT 403976-61-4  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,  
unclassified); NPO (Natural product occurrence); PRP (Properties); BIOL  
(Biological study); OCCU (Occurrence)  
(amino acid sequence; cDNA sequence of dysadherin, cancer-assocd. cell  
membrane glycoprotein, that down-regulates E-cadherin and promotes  
metastasis)
- IT 386529-39-1, GenBank AB072911  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)  
(nucleotide sequence; cDNA sequence of dysadherin, cancer-assocd. cell  
membrane glycoprotein, that down-regulates E-cadherin and promotes  
metastasis)

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Behrens, J; J Cell Biol 1989, V108, P2435 HCAPLUS
- (2) Braga, V; J Cell Biol 1997, V137, P1421 HCAPLUS
- (3) Chen, W; J Cell Biol 1991, V114, P319 HCAPLUS
- (4) Frixen, U; J Cell Biol 1991, V113, P173 HCAPLUS
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L78 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:756972 HCAPLUS

DN 133:320994

TI Improved method of identifying and locating immunobiologically-active  
linear peptides

IN Kokolus, William J.

PA USA

SO PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DT Patent  
 LA English  
 IC ICM G01N033-53  
 ICS C12P021-00; C07K001-00; A61K039-00  
 CC 15-2 (Immunochemistry)  
 Section cross-reference(s): 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000063693	A1	20001026	WO 2000-US10585	20000419
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1179178	A1	20020213	EP 2000-928224	20000419
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-130230P	P	19990420		
	US 2000-552461	A	20000418		
	WO 2000-US10585	W	20000419		
AB	<p>The present invention relates to identifying protein epitopes and more particularly to a novel method for identifying, detg. the location, optimal length of amino acid residues and immunobiol. potency of protein epitopes by fitting a hydrophilicity and/or hydrophobicity plot generated for the amino acid linear sequence of a polypeptide to a math. generated continuous curve thereby generating at least one set of potential epitopes which include ranked potential epitopes having a specific no. of amino acid residues. The immunobiol.-active linear peptides are deemed the potential epitopes that exhibit the most alternating positioning about an equil. position when juxtaposed on the hydrophilicity and/or hydrophobicity plot and their optimal length corresponds to the specific no. of amino acid residues in the set of ranked potential epitopes. The amino acid sequence of the protein epitopes of the present invention exhibit a hydrophobic-hydrophilic-hydrophobic motif. The method may be used to select hydrophobic-hydrophilic-hydrophobic epitopes from cancer cells, viral, microbial and other mols. of basic and clin. research interest in lymphokines and interferons, cluster differentiation antigen and MHC antigens, hormones and growth factors, tumor markers and tumor suppressors, oncogenes, viral antigens, and nuclear matrix proteins.</p>				
ST	antigen epitope identification; hydrphobicity hydrophilicity curve antigen protein motif				
IT	Hydrophilicity (Kyte-Doolittle hydropathy value; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)				
IT	Histocompatibility antigens RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (MHC (major histocompatibility complex); improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)				
IT	Animal virus Microorganism (antigen; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)				
IT	Mathematical methods (curve; improved method comprising math. generated				

curve for identifying and locating immunobiol.-active linear peptides)

IT Antigens  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(differentiation, cluster; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Reaction  
(equation; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Protein motifs**  
(hydrophobic-hydrophilic-hydrophobic; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Prostate-specific antigen  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(immunogenic epitope; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Antiserums  
Epitopes  
Hydrophobicity  
Tumor markers  
(improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Antigens  
Growth factors, animal  
Hormones, animal, biological studies  
Interferons  
Lymphokines  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Proteins, specific or class**  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(nuclear matrix-assocd.; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Gene  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(oncogene; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Diagnosis  
(testing; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Proteins, specific or class**  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(tumor suppressor; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Antigens**  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(tumor-assocd.; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT 75037-46-6, Gelonin  
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(immunogenic epitope; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (3) Kyte; J Mol Biol 1982, V157, P105 HCAPLUS

L78 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:764292 HCAPLUS

DN 132:22170

TI Identification of peptides with degenerate HLA-DR binding specificity

IN Sette, Alessandro; Southwood, Scott; Sidney, John

PA Epimmune, Inc., USA

SO PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-574

ICS G01N033-53; C12N007-00; A61K039-42; A61K039-395; A61K039-21;  
A61K039-29; C07K016-00

CC 15-2 (Immunochemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961916	A1	19991202	WO 1999-US12066	19990528
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2332786	AA	19991202	CA 1999-2332786	19990528
	AU 9942244	A1	19991213	AU 1999-42244	19990528
	EP 1080370	A1	20010307	EP 1999-926084	19990528
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2002516824	T2	20020611	JP 2000-551261	19990528
PRAI	US 1998-87192P	P	19980529		
	WO 1999-US12066	W	19990528		
AB	The authors analyzed the peptide binding specificity of a set of 13 different DR mols., representative of DR types common among the worldwide population. Detailed maps of secondary anchors and secondary interactions were derived for three of them (DR4w4, DR1 and DR7). Furthermore, the authors demonstrated that a set of at least seven different DR types share overlapping peptide binding repertoires; and consequently that broadly degenerate HLA DR binding peptides are a relatively common occurrence. This study also describes computerized procedures which should greatly assist in the task of identification of such degenerate peptides.				
ST	peptide epitope degeneracy HLA DR				
IT	Histocompatibility antigens				
	RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (HLA-DR, HLA-DR12; identification of peptides with degenerate HLA-DR binding specificity)				
IT	Histocompatibility antigens				
	RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (HLA-DR, HLA-DR13; identification of peptides with degenerate HLA-DR binding specificity)				
IT	Histocompatibility antigens				
	RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL				

(Biological study); PROC (Process)  
(HLA-DR, HLA-DR51; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR, HLA-DR53; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR1; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR2; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR3; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR4; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR6; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR7; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR8; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DR9; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(HLA-DRw11; identification of peptides with degenerate HLA-DR binding specificity)

IT **Peptides**, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(analog; with degenerate HLA-DR binding specificity)

IT T cell (lymphocyte)  
(cytotoxic; peptides with degenerate HLA-DR binding specificity for stimulation of)

IT Carcinoembryonic antigen  
neu (receptor)

p53 (**protein**)  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (degenerate HLA-DR binding specificity for peptides of)

IT Hepatitis B virus  
 Hepatitis C virus  
 Human immunodeficiency virus  
 Plasmodium falciparum  
 (degenerate HLA-DR binding specificity for peptides of antigens of)

IT Synthetic gene  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (for HLA-DR-restricted peptides)

IT **Algorithm**  
 (for identification of peptides with degenerate binding specificity for HLA-DR)

IT **Protein motifs**  
 (for peptides binding HLA-DR mols.)

IT T cell (lymphocyte)  
 (helper cell; peptides with degenerate HLA-DR binding specificity for stimulation of)

IT Epitopes  
 (identification of peptides with degenerate HLA-DR binding specificity)

IT Vaccines  
 (synthetic; peptides with degenerate HLA-DR binding specificity in relation to)

IT **Antigens**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (**tumor-assocd.**, MAGE-2; degenerate HLA-DR binding specificity for peptides of)

IT **Antigens**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (**tumor-assocd.**, MAGE-3; degenerate HLA-DR binding specificity for peptides of)

IT **Antigens**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (viral; degenerate HLA-DR binding specificity for peptides of)

IT **Peptides, biological studies**  
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
 (with degenerate HLA-DR binding specificity)

IT 165606-08-6 207344-41-0 207344-42-1 207344-43-2 207344-44-3  
 207344-45-4 207344-47-6 207344-48-7 207344-49-8 207344-50-1  
 207344-51-2 207344-53-4 207344-54-5 207344-55-6 207344-58-9  
 207344-59-0 207344-63-6 207344-64-7 211050-94-1 211051-04-6  
 211051-15-9 211051-25-1 211051-55-7 251545-14-9 251545-16-1  
 251545-17-2 251545-18-3 251545-20-7 251545-21-8 251545-22-9  
 251545-23-0 251545-24-1  
 RL: PRP (Properties)  
 (Unclaimed; identification of peptides with degenerate HLA-DR binding specificity)

IT 105250-02-0 117928-42-4 118174-51-9 119401-82-0 119586-94-6  
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 133561-13-4 133561-14-5 140457-64-3 140457-65-4 140457-70-1  
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RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (identification of peptides with degenerate HLA-DR binding specificity)

IT

251542-16-2	251542-17-3	251542-19-5	251542-20-8	251542-21-9
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251543-46-1	251543-49-4	251543-51-8	251543-52-9	251543-53-0
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251543-59-6	251543-60-9	251543-61-0	251543-62-1	251543-63-2
251543-64-3	251543-65-4	251543-66-5	251543-67-6	251543-68-7
251543-69-8	251543-70-1	251543-71-2	251543-72-3	251543-73-4
251543-74-5	251543-75-6	251543-77-8	251543-78-9	251543-79-0
251543-80-3	251543-81-4	251543-82-5	251543-83-6	251543-84-7
251543-85-8	251543-86-9	251543-87-0	251543-88-1	251543-89-2
251543-90-5	251543-92-7	251543-93-8	251543-94-9	251543-95-0
251543-96-1	251543-97-2	251543-98-3	251544-00-0	251544-01-1
251544-02-2	251544-03-3	251544-04-4	251544-05-5	251544-06-6
251544-08-8	251544-09-9	251544-10-2	251544-11-3	251544-12-4
251544-13-5	251544-14-6	251544-15-7	251544-16-8	251544-17-9
251544-18-0	251544-19-1	251544-20-4	251544-23-7	251544-25-9
251544-27-1	251544-29-3	251544-31-7	251544-33-9	251544-36-2
251544-40-8	251544-44-2	251544-45-3	251544-46-4	251544-47-5
251544-48-6	251544-49-7	251544-50-0	251544-51-1	251544-52-2
251544-53-3	251544-55-5	251544-56-6	251544-57-7	251544-58-8
251544-59-9	251544-60-2	251544-61-3	251544-63-5	251544-64-6
251544-65-7	251544-66-8	251544-67-9	251544-68-0	251544-69-1
251544-70-4	251544-71-5	251544-72-6	251544-74-8	251544-76-0
251544-77-1	251544-78-2	251544-79-3	251544-80-6	251544-81-7
251544-82-8	251544-83-9	251544-84-0	251544-85-1	251544-86-2
251544-87-3	251544-89-5	251544-90-8		

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(identification of peptides with degenerate HLA-DR binding specificity)

IT 251544-91-9 251544-92-0 251544-93-1 251544-94-2 251544-95-3  
251544-96-4 251544-97-5 251544-98-6 251545-00-3 251545-01-4  
251545-02-5 251545-03-6 251545-04-7 251545-05-8 251545-06-9  
251545-07-0 251545-08-1 251545-09-2 251545-11-6 251545-12-7  
251545-13-8 251661-56-0 251661-57-1 251661-58-2 251661-59-3  
251661-60-6 251661-64-0 251973-65-6

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(identification of peptides with degenerate HLA-DR binding specificity)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bremers; J Immunotherapy 1995, V18(2), P77 HCAPLUS
- (2) Fraziano; Clinical Immunology and Immunopathology 1997, V84(2), P202 MEDLINE
- (3) Harrison; J Exp Med 1997, V185(6), P1013 HCAPLUS
- (4) Ras; Human Immunology 1997, V53, P81 HCAPLUS
- (5) Valmori; Cancer Research 1997, V57(4), P735 HCAPLUS
- (6) Zaremba; Cancer Research 1997, V57, P4570 HCAPLUS

L78 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:639411 HCAPLUS

DN 127:306411

TI Molecular cloning of a monoclonal anti-tumor antibody specific for the Tn antigen and expression of an active single-chain Fv fragment

AU Babino, Alvaro; Pritsch, Otto; Oppezso, Pablo; Du Pasquier, Renaud; Roseto, Alberto; Osinaga, Eduardo; Alzari, Pedro M.

CS Departamento de Bioquimica, Facultad de Medicina, Montevideo, Urug.

SO Hybridoma (1997), 16(4), 317-324

CODEN: HYBRDY; ISSN: 0272-457X

PB Liebert

DT Journal

LA English

CC 15-3 (Immunochemistry)

Section cross-reference(s): 14

AB The authors report here the first amino acid sequence of an anti-Tn monoclonal antibody raised against human breast cancer cells

and show that a single chain Fv fragment of this IgM retains the Tn-binding specificity as defined by functional assays with asialo-OSM and membrane exts. from MCF-7 cells. Sequence comparisons and mol. modeling of 83D4 indicate that the antibody combining site displays a cavity-like feature primarily defined by the CDR H1 and H2 loops. This pocket could accommodate a single Tn mol., thus, suggesting a structural explanation for the predominant expression of a particular VH gene segment in a group of antibodies that recognize **tumor-assocd.**

**antigens** arising from an aberrant O-glycosylation.

- ST monoclonal antibody Tn tumor antigen; scFv antibody Tn breast tumor
- IT Gene, animal  
RL: PRP (Properties)  
(Igh; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT Gene, animal  
RL: PRP (Properties)  
(Ig.kappa.; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT Immunoglobulins  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(M, monoclonal; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT Blood-group substances  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(Tn; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT **DNA sequences**  
**Protein sequences**  
(cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT Immunoglobulins  
RL: PRP (Properties)  
(heavy chains, .mu.; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT Immunoglobulins  
RL: PRP (Properties)  
(light chains, .kappa.; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT Mammary gland  
(neoplasm; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT **Molecular modeling**  
(of monoclonal anti-Tn antibody)
- IT Antibodies  
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)  
(single chain, scFv; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)
- IT 14215-68-0D, .alpha.-N-Acetylgalactosamine, glycoproteins expressing  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

L78 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN 1986:219959 HCAPLUS

DN 104:219959

TI Primary structure of the human melanoma-associated antigen p97  
(melanotransferrin) deduced from the mRNA sequence

AU Rose, Timothy M.; Plowman, Gregory D.; Teplow, David B.; Dreyer, William

J.; Hellstroem, Karl Erik; Brown, Joseph P.  
 CS ONCOGEN, Seattle, WA, 98121, USA  
 SO Proceedings of the National Academy of Sciences of the United States of  
 America (1986), 83(5), 1261-5  
 CODEN: PNASA6; ISSN: 0027-8424  
 DT Journal  
 LA English  
 CC 3-3 (Biochemical Genetics)  
 Section cross-reference(s): 13, 14, 15  
 AB Cell-surface glycoprotein p97 is present in most human melanomas but only  
 in trace amts. in normal adult tissues. To det. the structure of this  
**tumor-assocd. antigen** and to identify its  
 functional domains, p97 mRNA was purified, cloned, and its nucleotide  
 sequence detd. The mRNA encodes a 738-residue precursor, which contains  
 the previously detd. N-terminal **amino acid** sequence of  
 p97. After removal of a 19-residue signal **peptide**, the mature  
 p97 mol. comprises **extracellular domains** of 342 and  
 352 residues and a C-terminal 25-residue stretch of predominantly  
 uncharged and hydrophobic **amino acids** which acts as a  
 membrane anchor. Each **extracellular domain** contains  
 14 cysteine residues, which form 7 intradomain disulfide bridges, and 1-2  
 potential N-**glycosylation** sites. Protease digestion studies  
 show that the 3 major **antigenic** determinants of p97 are present  
 on the N-terminal domain. The domains are strikingly homologous to each  
 other (46% **amino acid** sequence homol.) and to the  
 corresponding domains of human serum transferrin (39% homol.).  
 Conservation of disulfide bridges and of **amino acids**  
 thought to compose the iron-binding pockets suggests that p97 is also  
 related to transferrin in tertiary structure and function. Glycoprotein  
 p97 should be renamed melanotransferrin to denote its original  
 identification in melanoma cells and its evolutionary relationship to  
 serotransferrin and lactotransferrin, the other members of the transferrin  
 superfamily.  
 ST human melanoma glycoprotein p97 cDNA sequence; melanotransferrin gene  
 sequence human melanoma; cloning sequence glycoprotein p97 mRNA human  
 IT Melanoma  
 (antigen p97 of, of human, structure of)  
 IT Gene and Genetic element, animal  
 RL: BIOL (Biological study)  
 (for antigen p97, of human melanoma cell, nucleotide and encoded  
 peptide sequences of)  
 IT Transferrins  
 RL: BIOL (Biological study)  
 (glycoprotein antigen p97 of human melanoma structural homol. with)  
 IT **Protein** sequences  
 (of glycoprotein antigen p97 and precursor, of human melanoma,  
 complete)  
 IT Molecular cloning  
 (of glycoprotein antigen p97 cDNA, of human melanoma cells)  
 IT Ribonucleic acids, messenger  
 RL: PROC (Process)  
 (antigen p97-specifying, of human melanoma cells, purifn. of)  
 IT **Deoxyribonucleic acid** sequences  
 (antigen p97-specifying, of human, complete)  
 IT Transferrins  
 RL: BIOL (Biological study)  
 (melano-, glycoprotein antigen p97 of human melanoma as)  
 IT Antigens  
 RL: BIOL (Biological study)  
 (p97, of human melanoma cells, structure of)  
 IT 102347-16-0 102347-17-1  
 RL: PRP (Properties)  
 (amino acid sequence of)

IT 102347-28-4  
RL: PRP (Properties); BIOL (Biological study)  
(nucleotide sequence of)

=> fil medline  
FILE 'MEDLINE' ENTERED AT 15:13:54 ON 19 NOV 2002

FILE LAST UPDATED: 16 NOV 2002 (20021116/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

If you received SDI results from MEDLINE on October 8, 2002, these may have included old POPLINE data and in some cases duplicate abstracts. For further information on this situation, please visit NLM at:  
[http://www.nlm.nih.gov/pubs/techbull/so02/so02\\_popline.html](http://www.nlm.nih.gov/pubs/techbull/so02/so02_popline.html)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L121 ANSWER 1 OF 4 MEDLINE  
AN 2002325926 MEDLINE  
DN 22045525 PubMed ID: 12050499  
TI Evaluation of a new serum testing method for detection of prostate cancer.  
AU Seabury Charles A; Calenoff Emanuel; Ditlow Charles;  
Bux Sajit; Clarke Harry; Issa Muta; Marshall Fray; Petros John  
CS Emory University, Atlanta, Georgia, USA.  
SO JOURNAL OF UROLOGY, (2002 Jul) 168 (1) 93-9.  
Journal code: 0376374. ISSN: 0022-5347.  
CY United States  
DT (EVALUATION STUDIES)  
Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 200207  
ED Entered STN: 20020619  
Last Updated on STN: 20020709  
Entered Medline: 20020708  
AB PURPOSE: Serum prostate specific antigen is a highly specific test for diseases of the prostate gland but it is not specific for prostate cancer, which can lead to unnecessary biopsies. In an effort to find a more specific test, a new testing method for detecting prostate cancer based on deglycosylation of cell surface proteins and subsequent antibody formation in patients with prostate cancer was evaluated. In addition, antibody generation against the peptide fragments chosen to represent the cell surface proteins was determined to be cancer associated, cancer specific or not related to prostate cancer. MATERIALS AND METHODS: Antibody titers to 67 unique peptide sequences representing 41 cell surface proteins were

determined in 25 men with known prostate cancer (cancer group) and 34 men without prostate cancer (control group). The titers of the control and cancer groups were compared for statistical significance. Additionally, each peptide was identified as being **cancer specific**, **cancer associated** or not related to prostate cancer based on whether patients, controls, both or neither had elevated antibody titers. RESULTS: Of the 67 peptides tested 3 demonstrated statistical significance between the control and cancer group titers. Using these 3 informative peptides, 11 of the 25 men known to have prostate cancer had positive results (sensitivity 44%), while 2 of the 34 control patients had positive results (specificity 94%). Of the peptides with significantly different titers in patients and controls 2 of the 19 cell surface proteins known to be present in prostate cancer were represented. No peptides were found to generate antibodies only in patients with cancer (**cancer specific**), while 3 were **cancer associated** (increased in cancer and controls). CONCLUSIONS: A new approach to testing for prostate cancer, although lacking in sensitivity, appears to be highly specific. The high specificity of this test suggests that when combined with a highly sensitive test, such as prostate specific **antigen**, screening could be significantly improved.

CT Check Tags: Comparative Study; Human; Male

Adult

Aged

\*Antibodies, Neoplasm: BL, blood

Antibody Specificity: IM, immunology

\*Antigens, Surface: BL, blood

Biopsy

Middle Age

\*Peptide Fragments: BL, blood

Predictive Value of Tests

Prostate: PA, pathology

Prostate-Specific Antigen: BL, blood

\*Prostatic Neoplasms: DI, diagnosis

Prostatic Neoplasms: IM, immunology

Reference Values

\*Tumor Markers, Biological: BL, blood

CN 0 (Antibodies, Neoplasm); 0 (Antigens, Surface); 0 (Peptide Fragments); 0 (Tumor Markers, Biological); EC 3.4.21.77 (Prostate-Specific Antigen)

L121 ANSWER 2 OF 4 MEDLINE

AN 2000463821 MEDLINE

DN 20468866 PubMed ID: 11016651

TI Use of two predictive algorithms of the world wide web for the identification of tumor-reactive T-cell epitopes.

AU Lu J; Celis E

CS Department of Immunology and Cancer Center, Mayo Clinic and Mayo Graduate School, Rochester, Minnesota 55905, USA.

NC R01CA80782 (NCI)

SO CANCER RESEARCH, (2000 Sep 15) 60 (18) 5223-7.

Journal code: 2984705R. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200010

ED Entered STN: 20001027

Last Updated on STN: 20001027

Entered Medline: 20001013

AB Tumor cells can be effectively recognized and eliminated by CTLs. One approach for the development of CTL-based cancer immunotherapy for solid tumors requires the use of the appropriate immunogenic peptide epitopes that are derived from defined **tumor-associated antigens**. Because CTL peptide epitopes are restricted to specific

MHC alleles, to design immune therapies for the general population it is necessary to identify epitopes for the most commonly found human MHC alleles. The identification of such epitopes has been based on MHC-peptide-binding assays that are costly and labor-intensive. We report here the use of two computer-based prediction algorithms, which are readily available in the public domain (Internet), to identify HLA-B7-restricted CTL epitopes for carcinoembryonic **antigen** (CEA). These algorithms identified three candidate peptides that we studied for their capacity to induce CTL responses in vitro using lymphocytes from HLA-B7+ normal blood donors. The results show that one of these peptides, CEA9(632) (IPQQHTQVL) was efficient in the induction of primary CTL responses when dendritic cells were used as **antigen**-presenting cells. These CTLs were efficient in killing tumor cells that express HLA-B7 and produce CEA. The identification of this HLA-B7-restricted CTL epitope will be useful for the design of ethnically unbiased, widely applicable immunotherapies for common solid epithelial tumors expressing CEA. Moreover, our strategy of identifying MHC class I-restricted CTL epitopes without the need of peptide/HLA-binding assays provides a convenient and cost-saving alternative approach to previous methods.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

**\*Algorithms**

Amino Acid Sequence

Antibodies, Monoclonal: IM, immunology

Antigen Presentation: IM, immunology

**\*Carcinoembryonic Antigen: IM, immunology**

Carcinoembryonic Antigen: ME, metabolism

Cell Line, Transformed

Dendritic Cells: IM, immunology

**\*Epitopes, T-Lymphocyte: IM, immunology**

**\*HLA-B7 Antigen: IM, immunology**

HLA-B7 Antigen: ME, metabolism

Immunotherapy, Adoptive

**\*Internet**

Lymphocyte Transformation: IM, immunology

Neoplasms: IM, immunology

Neoplasms: TH, therapy

**\*Peptide Fragments: IM, immunology**

Peptide Fragments: ME, metabolism

Predictive Value of Tests

T-Lymphocytes, Cytotoxic: IM, immunology

Tumor Cells, Cultured

CN 0 (Antibodies, Monoclonal); 0 (Carcinoembryonic Antigen); 0 (Epitopes, T-Lymphocyte); 0 (HLA-B7 Antigen); 0 (Peptide Fragments)

L121 ANSWER 3 OF 4 MEDLINE

AN 97384957 MEDLINE

DN 97384957 PubMed ID: 9242452

TI T-cell recognition of tumor-associated carbohydrates: the nature of the glycan moiety plays a decisive role in determining glycopeptide immunogenicity.

AU Galli-Stampino L; Meinjohanns E; Frische K; Meldal M; Jensen T; Werdelin O; Mouritsen S

CS M&E Biotech A/S, Valby, Denmark.

SO CANCER RESEARCH, (1997 Aug 1) 57 (15) 3214-22.

Journal code: 2984705R. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199709

ED Entered STN: 19970922

Last Updated on STN: 19970922

Entered Medline: 19970911

AB Aberrant glycosylation is one of the most constant traits of the malignant cell phenotype. To study T-cell responses to **tumor-associated** glycans, the mouse hemoglobin-derived decapeptide Hb(67-76), which binds well to the MHC class II molecule E(k) and is nonimmunogenic in CBA/J mice, was either O- or N-glycosylated at its primary T-cell receptor contact residue, position 72, with different glycans attached to either threonine, serine, or asparagine. The carbohydrate moieties included **tumor-associated** mucins, i.e., the Tn and T **antigens**, mucin-related glycans, and mucin-unrelated glycans. The side chain of the amino acid in position 72 points away from the MHC binding site when the Hb(67-76) peptide is bound to E(k), so the assumption was that this was also the case for glycans attached to this position. The glycosylated Hb(67-76) peptide analogues were then studied for binding to E(k) and for immunogenicity in CBA/J mice. All 16 glycopeptides bound well to E(k), although those with the more complex carbohydrates bound more weakly than those with monosaccharides. Six of 12 O-glycosylated and 0 of 4 N-glycosylated glycopeptides were able to induce a T-cell proliferative response with a stimulation index above 3.0. Some glycopeptides were not immunogenic, suggesting that there may be holes in the T-cell repertoire due to a lack of T-cell receptor regions accommodating certain glycan structures. The four strongest immunogenic glycopeptides were all O-glycosylated, and interestingly, three of them carried the **tumor-associated** Tn or T **antigen**. On the other hand, the Hb(67-76) peptide analogue with the natural mucin Core2 structure attached did not elicit any T-cell response. T cells primed to a glycopeptide with a simple glycan structure such as Tn did not cross-respond significantly to other glycopeptides, indicating a high degree of carbohydrate specificity in T-cell recognition. T cells primed to a glycopeptide carrying the more complex T **antigen** showed a complicated pattern of cross-responses to glycopeptides with simpler glycan moieties. The fact that it is possible to raise MHC class II-restricted T-cell responses against **tumor-associated** carbohydrate structures opens new perspectives for the designing of cancer vaccines.

CT Check Tags: Animal; Support, Non-U.S. Gov't

\*Antigens, Tumor-Associated, Carbohydrate: IM, immunology

Binding, Competitive

Cell Division: IM, immunology

\*Glycopeptides: IM, immunology

\*Hemoglobins: ME, metabolism

\*Histocompatibility Antigens Class II: ME, metabolism

Mice

Mice, Inbred CBA

Models, Structural

\*Peptide Fragments: IM, immunology

\*T-Lymphocytes: IM, immunology

T-Lymphocytes: ME, metabolism

CN 0 (Antigens, Tumor-Associated, Carbohydrate); 0 (Glycopeptides); 0 (Hemoglobins); 0 (Histocompatibility Antigens Class II); 0 (Peptide Fragments)

L121 ANSWER 4 OF 4 MEDLINE

AN 95142964 MEDLINE

DN 95142964 PubMed ID: 7840926

TI Serum immunoglobulins specific for intracellular proteins of squamous cell carcinoma.

AU Calenoff E; Cheever M A; Satam M; Dutra J C; Pelzer H J; Kern R C; Hanson D G

CS Department of Otolaryngology and Head and Neck Surgery, Northwestern University Medical School, Chicago, Ill.

SO ARCHIVES OF OTOLARYNGOLOGY -- HEAD AND NECK SURGERY, (1995 Feb) 121 (2) 183-91.

Journal code: 8603209. ISSN: 0886-4470.

CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 199503  
ED Entered STN: 19950316  
Last Updated on STN: 19970203  
Entered Medline: 19950309

AB OBJECTIVE: To determine an autologous humoral immune response to squamous cell carcinoma (SCC) intracellular proteins in patients with SCC. DESIGN: Intracellular proteins were isolated from 25 different cultured SCC lines. The proteins were used as a source of **antigens** to measure IgA, IgE, and IgG responses in the serum samples of patients and controls. Antibody response was assessed in both unfractionated and fractionated intracellular proteins. PATIENTS: The serum samples of 65 patients with SCC and of 65 age- and gender-matched controls were tested. RESULTS: Antibodies to SCC intracellular proteins were detected in the serum samples of 40 (62%) of the 65 patients with SCC and in the serum samples of 46 (71%) of 65 controls. Thirty (46%) of the patients with SCC and 40 (62%) of the controls had IgE responses, 18 (28%) of the patients and one (2%) of the controls had IgA responses, and 17 (26%) of the patients and 14 (22%) of the controls had IgG responses. An inverse relation was noted between detectable IgE responses and IgA or IgG responses in the patients and the controls. The analysis of antibody response indicated that 28 molecules were recognized predominantly by the serum samples of patients with SCC, but not by the serum samples of controls. CONCLUSIONS: A substantial proportion of patients with SCC and of controls exhibited an autologous humoral immune response to SCC intracellular proteins. The IgE responses to SCC intracellular proteins were inversely related to IgA or to IgG responses. Different antibody isotypes normally cause markedly different immune functions, and may suggest different roles for the existent immune responses to SCC **antigens**. We identified many **tumor-associated antigens** that were selectively recognized by the serum samples of patients with SCC. These **antigens** could be used to define molecular studies of immune surveillance and selection, and may represent appropriate targets for immunotherapy.

CT Check Tags: Human  
Autoradiography  
Blotting, Western  
\*Carcinoma, Squamous Cell: IM, immunology  
\*Head and Neck Neoplasms: IM, immunology  
Immunoglobulin A: BL, blood  
Immunoglobulin E: BL, blood  
Immunoglobulin G: BL, blood  
\*Immunoglobulins: BL, blood  
Immunoglobulins: ME, metabolism  
Neoplasm Proteins: IM, immunology  
Neoplasm Proteins: ME, metabolism  
Tumor Cells, Cultured

RN 37341-29-0 (Immunoglobulin E)  
CN 0 (Immunoglobulin A); 0 (Immunoglobulin G); 0 (Immunoglobulins); 0 (Neoplasm Proteins)

=> fil wpix

FILE 'WPIX' ENTERED AT 15:23:13 ON 19 NOV 2002

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FILE LAST UPDATED: 18 NOV 2002 <20021118/UP>  
MOST RECENT DERWENT UPDATE: 200274 <200274/DW>  
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=> d all abeq tech abex tot 1136

L136 ANSWER 1 OF 3 WPIX (C) 2002 THOMSON DERWENT

AN 2002-566624 [60] WPIX

DNC C2002-160592

TI Candidates for cancer-specific or cancer-associated antigens useful for diagnosis and treatment of cancer comprise synthetic peptides.

DC B04

IN CALENOFF, E; DITLOW, C C

PA (NOUN) UNIV NORTHWESTERN

CYC 98

PI WO 2002047613 A2 20020620 (200260)\* EN 53p A61K000-00

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002043314 A 20020624 (200267) A61K000-00

ADT WO 2002047613 A2 WO 2001-US47734 20011113; AU 2002043314 A AU 2002-43314 20011113

FDT AU 2002043314 A Based on WO 200247613

PRAI US 2000-723307 20001127

IC ICM A61K000-00

AB WO 200247613 A UPAB: 20020919

NOVELTY - Identifying candidates that are cancer-specific or cancer-associated antigens involves:

- (1) mapping hydrophilic regions of amino acid sequences;
- (2) identifying hydrophilic peptide regions that are glycosylated in non-cancerous cells, but deglycosylated in cancer cells; and
- (3) synthesizing, labeling and testing peptides.

DETAILED DESCRIPTION - Identifying candidates that are cancer-specific or cancer-associated antigens involves:

- (a) obtaining the amino acid sequences of the extracellular domain of a receptor or receptor-like molecule;
- (b) mapping hydrophilic regions of the domain by analyzing the amino acid sequence of the domain employing the rolling sum analysis of seven consecutive residues;
- (c) identifying the hydrophilic peptide regions of step (b) that are glycosylated in non-cancerous (normal) cells, but are deglycosylated in cancer cells;
- (d) locating amino acids that are susceptible to modification in the absence of steric hindrance by glycoside chains;
- (e) synthesizing candidate peptides that fit the criteria of steps (a) to (d);

(f) labeling the peptides at either end of their amino acid sequence;  
and

(g) testing whether the candidate peptides are cancer-specific or cancer associated.

INDEPENDENT CLAIMS are included for the following:

(1) a cancer-specific or highly cancer-associated peptide comprising an amino acid sequence containing 3 - 1000 amino acids; a net hydrophilic character; and at least one glycosylatable amino acid located at no further than 3 amino acids away from the amino acid adjacent to either end of the peptide;

(2) an immunogenic composition comprising the peptide and capable of inducing a mammal to produce antibodies specific for an epitope on a cancer cell;

(3) an immunoassay by determining whether the peptide has complexed with an antibody in the biological fluids;

(4) a diagnostic method involving placing several peptides in a microchip to detect cancer in a subject from which a biological sample is obtained, and detecting the cancer by hybridization of antibodies in the biological sample;

(5) a molecule (I) specifically reactive with the peptide, selected from monoclonal antibodies or their immunogenic fragments, recombinant proteins or adhesion proteins;

(6) delivering cancer cell molecules containing epitopes expressed by the peptides for identifying cancer status by an immunoassay for the complexing of the cancer cell with (I);

(7) determining degree of cancer expression or by measuring antibody by the immunoassay;

(8) determining type of cancer cells in a biological sample by complexing of cancer cell molecules with (I);

(9) a cancer imaging reagent comprising (I) and a label;

(10) a therapeutic construct (C1) comprising the peptide, and an adjuvant/peptide conjugates comprising the peptide coupled to a molecule which facilitates enhanced immunogenicity, and neomolecules created by recombinant techniques containing a peptide with adjuvant molecular sequences which promotes increased immunogenicity of the peptide;

(11) a therapeutic construct (C2) comprising a nucleic acid molecule comprising a nucleotide sequence encoding the peptide, expressed as the protein or peptide by the cells of an individual after administration, to cause auto-stimulation of the individuals immune system; and

(12) producing immunity to cancer by administering (C2) to a mammal.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Cancer cell apoptosis promoter.

USE - To identifying candidates that are cancer-specific or cancer-associated antigens for use in the diagnosis and treatment of cancer (claimed)

ADVANTAGE - The method involves the use of a site of deglycosylated amino acid in the cancer cells, thus conferring a cancer-specific or highly cancer-associated immunogenicity or marker function to the peptide and avoiding self-recognition, compared to the prior art peptides. The peptides are further not intracellularly expressed, but are located on the cell surfaces (predictably secreted or released into pericellular fluids) in sufficient numbers, thus are sufficiently accessible for targeting T cells; and are present at the earlier stages of cancer progression as well as during later stages; and are retained on the surface of the cancer cells for a time sufficient for the therapeutic T cells to find their target and retain the bound T cells for a time sufficient to affect cancer cell death.

Dwg.0/1

FS

CPI

FA

AB; DCN

MC

CPI: B04-B04C; B04-C01; B04-K01;

B04-N02; B10-B02; B11-C07B5; B11-C08A; B12-K04A1;

B14-H01B; B14-H03

TECH

UPTX: 20020919

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Peptides: The peptide is immunogenic. The glycosylatable amino acid is asparagine. The peptide further comprising several deglycosylated amino acids, each separated from the deglycosylated amino acid nearest to it by not more than 6 unmodified amino acids. The peptide further comprises: a chemical modification of at least one of the deglycosylated amino acids, such that the chemical modification confers upon the peptide an additional cancer-specific or highly cancer-associated immunogenicity than that due to glycosylation; and an amino acid sequence with not more than 3 unmodified amino acids are located on either side of a modified amino acid or amino acid that has a glycosylation site removed. The chemical modification is phosphorylation. The peptide is produced synthetically.

Preferred Label: The label is radioisotopic and, upon binding to cancer cells cancerous lesion, highlights the presence of the cancer cells when scanned with a nuclear medicine scanner. The cancer imaging reagent contains a paramagnetic label which, upon binding to cancer cells highlights the presence of the cancer cells when scanned with a nuclear magnetic resonance (NMR) scanner; or a water density label which, upon binding to cancer cells highlights the presence of the cancer cells when scanned with a CAT scanner.

Preferred Therapeutic Agents: The cancer therapeutic reagents bind to a cancer cell and promote lysis of that cell; bind to and block the function of a receptor or receptor-like molecule or adhesion molecule on a cancer cell, so as to promote a reduction or cessation of cancer cell growth or migration, or promote cancer cell death; and carry a radioisotope or a toxin which upon binding to a cancer cell damages or promotes cancer cell death.

ABEX

SPECIFIC SEQUENCES - Thirty sequences of amino acids are specifically claimed as suitable candidate cancer antigens, e.g. (uuMuuN)<sub>n</sub> where u is an unmodified amino acid, N is a deglycosylation amino acid, M is a modified amino acid and n is number of repeats of a basic unit.

EXAMPLE - No relevant example given.

L136 ANSWER 2 OF 3 WPIX (C) 2002 THOMSON DERWENT

AN 2000-579032 [54] WPIX

DNC C2000-172270

TI Novel composition comprising deglycosylated fragments of kringle 1-5 regions of plasminogen linked to the glycosylated form, useful for inhibiting angiogenesis.

DC B04 C06 D16

IN FOLKMAN, M J; LIANG, H; MACDONALD, N J; PIRIE-SHEPHERD, S; SIM, K L

PA (CHIL-N) CHILDRENS MEDICAL CENT; (ENTR-N) ENTREMED INC

CYC 90

PI WO 2000047729 A1 20000817 (200054)\* EN 42p C12N009-68

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES  
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS  
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL  
TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000029903 A 20000829 (200062) C12N009-68

EP 1153125 A1 20011114 (200175) EN C12N009-68

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 2002536458 W 20021029 (200274) 49p A61K038-48

ADT WO 2000047729 A1 WO 2000-US3482 20000210; AU 2000029903 A AU 2000-29903  
20000210; EP 1153125 A1 EP 2000-908590 20000210, WO 2000-US3482 20000210;  
JP 2002536458 W JP 2000-598628 20000210, WO 2000-US3482 20000210

FDT AU 2000029903 A Based on WO 200047729; EP 1153125 A1 Based on WO  
200047729; JP 2002536458 W Based on WO 200047729

PRAI US 1999-128062P 19990407; US 1999-119562P 19990210

IC ICM A61K038-48; C12N009-68  
 ICS A61K038-49; A61P015-00; A61P017-06; A61P027-02; A61P029-00;  
 A61P035-00; A61P035-02; A61P035-04; A61P043-00; C07K014-745;  
 C12N015-09

AB WO.200047729 A UPAB: 20011129  
 NOVELTY - Composition comprising a deglycosylated fragment (I) of a  
 kringle 1-5 region of a plasminogen (PG) protein that lacks at least 1  
 carbohydrate moiety linked to (and in a greater amount than) the naturally  
 glycosylated form, where the deglycosylated fragment has antiangiogenic  
 activity, is new.  
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the  
 following:  
 (1) a nucleotide sequence (II) encoding the deglycosylated fragment  
 of (I);  
 (2) a deglycosylated fragment of a kringle 1-5 region of a PG protein  
 comprising a sequence of 260 amino acids (aa) (Ia), given in the  
 specification; and  
 (3) a nucleic acid encoding a deglycosylated fragment of a kringle  
 1-5 region of a PG protein comprising a sequence of 1679 base pairs (bp)  
 (IIa), given in the specification.  
 ACTIVITY - Cytostatic; antiangiogenic.  
 No biological data given.  
 MECHANISM OF ACTION - Angiostatin agonist.  
 USE - The compositions are useful for inhibiting angiogenesis  
 (claimed)  
 DESCRIPTION OF DRAWING(S) - The diagram shows the inhibition of  
 endothelial cell proliferation by glycosylated and deglycosylated kringle  
 1-5 region proteins.  
 Dwg.4/4

FS CPI  
 FA AB; GI; DCN  
 MC CPI: B04-B03B; B04-C01G; B04-E02B; B04-H01; B04-H0100E; B04-H15;  
 B04-H1500E; B04-N02A; B14-H01B; B14-L06; C04-B03B; C04-C01G;  
 C04-E02B; C04-H01; C04-H0100E; C04-H15; C04-H1500E; C04-N02A;  
 C14-H01B; C14-L06; D05-C12; D05-H12A; D05-H12B; D05-H17A2; D05-H17A6;  
 D05-H17B2; D05-H17B6

TECH UPTX: 20001027  
 TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fragments: (I) lacks a  
 bisialylated-biantennary glycan, an N-linked carbohydrate moiety, and/or a  
 carbohydrate chain at aa Asn289 of human PG (hPG). The fragment is a  
 kringle 1-3 protein. The fragment begins at aa 87 of hPG and preferably  
 comprises (Ia). The fragment has a substitution at aa 289 of hPG. (I) has  
 antiangiogenic activity in vitro and/or in vivo.  
 Production: The deglycosylated fragment is produced recombinantly.  
 Preferred Composition: The composition has a ratio of deglycosylated  
 fragment to glycosylated form of at least 60:40 (preferably 100:0).  
 Preferred Nucleotide: The nucleotide of (II) is (IIa).

ABEX  
 EXAMPLE - Human plasminogen (hPG) was purified from human plasma according  
 to Brockway W. J. and Castellino, F. J., Arch. Biochem. Biophys.  
 151:194-199 (1972). The hPG was then applied to a 5 ml conA HiTrap column.  
 PG2 (deglycosylated) does not bind to the column, which was rinsed with 5  
 column volumes of equilibration buffer (50 mM Tris (RTM) pH7.5/ 1 mM  
 MgCl2/ 1 mM CaCl2) and PG1 (glycosylated) eluted. PG1 and 2 were dialyzed  
 against 20 mM Tris (RTM) pH 7.6 and equal amounts of the glycoforms were  
 then digested with porcine pancreatic elastase (PPE) as in O'Reilly, M. S.  
 et al. Nature Medicine 2:689-692 (1996). The kringle 1-3 region protein  
 was separated from the kringle 4 and other smaller (less than 12 kDa)  
 fragments by gel filtration. Bovine capillary endothelial cells were  
 maintained in Dulbecco's modified Eagle's medium/minimal essential medium  
 (DMEM) with 10 % heat-inactivated BCS (not defined), antibiotics and 3  
 ng/ml recombinant human bFGF (fibroblast growth factor). Cells were washed  
 with phosphate buffered saline (PBS) and dispersed in a 0.05 % solution of

trypsin. A cell suspension was made with DMEM/ 10 % BCS/ 1 % antibiotics and adjusted to 25000 cells/ml. Cells were plated onto gelatinized culture plates and incubated 37 degrees C in 10 % CO2 for 24 hours. The media was then replaced with 0.25 ml of DMEM/ 1% BCS/ 1 % antibiotics and the test sample (PG1 or PG2) applied. After 20 minutes incubation media and bFGF were added. After a further 72 hours the cells were dispersed in trypsin, resuspended and then counted. The assays shows that PG2 isoforms have a higher inhibitory effect on epithelial cells than PG1.

L136 ANSWER 3 OF 3 WPIX (C) 2002 THOMSON DERWENT

AN 1999-244276 [20] WPIX

DNC C1999-071294

TI Liquid formulation of interferon-beta.

DC A96 B04

IN HOFER, H; SCHROEDER, P; SIKLOSI, T; TSCHOEPE, M

PA (RENT) RENTSCHLER BIOTECHNOLOGIE GMBH

CYC 25

PI WO 9915193 A1 19990401 (199920)\* DE 51p A61K038-21

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU CA IL JP KR US

AU 9896276 A 19990412 (199934)

EP 1017413 A1 20000712 (200036) DE A61K038-21

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

KR 2001015599 A 20010226 (200156) A61K038-21

JP 2001517635 W 20011009 (200174) 47p A61K038-21

AU 741300 B 20011129 (200206) A61K038-21

EP 1224940 A1 20020724 (200256) DE A61K038-21

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

EP 1017413 B1 20020925 (200271) DE A61K038-21

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT WO 9915193 A1 WO 1998-EP6065 19980923; AU 9896276 A AU 1998-96276 19980923; EP 1017413 A1 EP 1998-950074 19980923, WO 1998-EP6065 19980923; KR 2001015599 A KR 2000-703036 20000322; JP 2001517635 W WO 1998-EP6065 19980923, JP 2000-512562 19980923; AU 741300 B AU 1998-96276 19980923; EP 1224940 A1 Div ex EP 1998-950074 19980923, EP 2002-4883 19980923; EP 1017413 B1 EP 1998-950074 19980923, WO 1998-EP6065 19980923, Related to EP 2002-4883 19980923

FDT AU 9896276 A Based on WO 9915193; EP 1017413 A1 Based on WO 9915193; JP 2001517635 W Based on WO 9915193; AU 741300 B Previous Publ. AU 9896276, Based on WO 9915193; EP 1224940 A1 Div ex EP 1017413; EP 1017413 B1 Related to EP 1224940, Based on WO 9915193

PRAI EP 1997-116562 19970923

IC ICM A61K038-21

ICS A61K009-08; A61K047-18

AB WO 9915193 A UPAB: 19990525

NOVELTY - Stable interferon- beta (I) solution of neutral or slightly acid pH (pH 5-8) is new.

DETAILED DESCRIPTION - Liquid formulations of human (I), that retain at least 80% of in vitro biological activity after storage for 3 months at 25 deg. C, contain up to 25 MU (units)/ml of (I), are buffered to pH 5-8, preferably over 5.5, and are free of human serum albumin (HSA); are buffered to pH 6-7.2 and are free of HSA, or are buffered to pH 5-8, preferably over 5.5, and contain at least one amino acid.

ACTIVITY - Antiviral; antiproliferative; immunomodulatory.

MECHANISM OF ACTION - None given.

USE - Interferons are known as antiviral, antiproliferative and immunomodulatory agents.

ADVANTAGE - The formulations have high stability (of biological activity and of molecular and physical integrity); eliminate the expense of freeze-drying and reconstitution, and do not require potentially hazardous additives (serum albumin or detergents). They may even be stored for a month at 37 deg. C and still retain at least 70% of biological activity. A formulation, of pH 7, contained 50 mM sodium phosphate, 50

mg/ml glycerol, 2 mM methionine and 12.5 MU/ml (I). After 6 months storage at 25 deg. C, recovery of biological activity (assessed conventionally by inhibition of the cytopathic effect of a virus) was 13.4 MU/ml, i.e. 107.2% of the initial value and 172% of a control that had been stored for 6 months at -20 deg. C.

Dwg.0/0 .

FS

CPI

FA

AB; DCN

MC

CPI: A12-V01; B04-H05B; B14-A02; B14-G03; B14-H01

TECH

UPTX: 19990517

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred buffer: This is phosphate, citrate and/or acetate at concentration 0.01-1, particularly 0.02-0.2 M, especially phosphate/citrate to provide pH 6-7.2, especially 6.2-6.8.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred materials: (I) is a glycosylated protein, particularly recombinant material from Chinese hamster ovary cells.

Preferred composition: This is free of HSA, surfactants and, apart from (I), polypeptides of human or animal origin, but may also contain at least one amino acid, particularly methionine at 0.1-4, especially 2 mM. Optionally the formulation also contains at least one agent to adjust osmotic pressure (e.g. mannitol or glycerol); a thickener (e.g. methylcellulose) and a preservative (e.g. thiomersal). Compositions retain chemical integrity (against polypeptide cleavage, oxidation and deglycosylation) and physical integrity (as measured from transmission at 420 nm) after storage for 6 months at 25 degrees Centigrade, and at least 85% of the original biological activity. Preferably the (I) concentration is 3-10 MU/ml.

ABEX

ADMINISTRATION - Formulations are administered orally, parenterally or ophthalmologically at unit doses of 1-25 MU (units).

=> d his

(FILE 'HOME' ENTERED AT 13:45:30 ON 19 NOV 2002)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:45:48 ON 19 NOV 2002

E CALENOFF E/AU

L1

21 S E4,E5

E DITLOW C/AU

L2

9 S E3-E5

E ENTERON/PA,CS

L3

3 S E3-E10

L4

28 S L1-L3

L5

28 S ROLL?(L)SUM(L)ANALY?

L6

0 S (ROLL OR ROLLED OR ROLLING)()SUM

L7

14 S (ROLL OR ROLLED OR ROLLING)(5A)SUM

L8

14 S L7 NOT L5

E MATHEMATICS/CT

L9

10519 S E3-E37

E E3+ALL

L10

10519 S E1

E E2+ALL

L11

10890 S E3-E5

L12

85709 S E2+NT

E MATH/CT

L13

6100 S E10-E38

E E39+ALL

E E2+ALL

L14

224812 S E2+NT

L15

65522 S E3-E5

```

      E STATISTIC/CT
L16      8813 S E47-E72
      E E5+ALL
L17      9265 S E4-E6
L18      14026 S E3+NT
      E E46+ALL
L19      1092 S E2,E3,E1
      E E5+ALL
L20      36057 S E2,E1+NT
L21      123450 S E7+NT OR E9+NT OR E11+NT OR E12+NT OR E15+NT OR E17+NT
      E E7+ALL
L22      70 S E4
      E E6+ALL
L23      36057 S E2 OR E1+NT
      E E8+ALL
L24      1019 S E4,E3+NT
      E E5+ALL
L25      2826 S E1
      E COMPUTER PROGRAMCT
      E COMPUTER PROGRAM/CT
      E E5+ALL
L26      3710 S E1
      E E2+ALL
L27      49668 S E1
L28      1 S L4 AND L9-L27
      E PROTEIN MOTIF/CT
      E E4+ALL
L29      35999 S E4+NT
L30      20443 S (PROTEIN# OR PEPTIDE# OR POLYPEPTIDE# OR AMINOACID# OR AMINO
L31      2215 S (PROTEIN# OR PEPTIDE# OR POLYPEPTIDE# OR AMINOACID# OR AMINO
L32      6211 S EXTRACELL? DOMAIN
L33      451 S L32 AND L30
L34      63 S L32 AND L31
L35      773 S L29 AND L32
L36      31 S L33-L35 AND L9-L27
      E SIMULATION/CT
L37      236446 S E3,E5,E6
      E E3+ALL
      E E2+ALL
L38      71733 S E3-E5,E2+NT
      E SIMULATION/CT
      E E5+AKK
      E E3+ALL
L39      235130 S E1
L40      9 S L33-L35 AND L37-L39
L41      35 S L36,L40
L42      7 S L41 AND ANTIGEN?
L43      7 S L41 AND (?CANCER? OR ?NEOPLAS? OR ?TUMOR? OR ?TUMOUR? OR ?MAL
L44      923440 S (PROTEIN# OR PEPTIDE#)/CW
L45      149277 S (AMINO(L)ACID#)/CW
L46      107917 S (AMINO ACID# OR PROTEIN# OR PEPTIDE#)/SC,SX
L47      2955 S L44-L46 AND L32
      E MOLECULAR STRUCTURE/CT
      E E3+ALL
L48      240580 S E2,E1+NT AND L44-L46
L49      15577 S (E232+NT OR E233+NT OR E234+NT OR E236+NT OR E240+NT OR E241+
L50      1530 S E225+NT AND L44-L46
L51      10215 S L47-L50 AND L9-L27
L52      109 S L51 AND GLYCOSYLAT?
L53      13 S L51 AND DEGLYCOSYLAT?
L54      10 S L52 AND L53
      SEL DN AN 2 6
L55      2 S L54 AND E1-E6

```

L56 2 S L28,L55  
 L57 1 S L42,L43 AND L56  
 L58 11 S L42,L43 NOT L56  
 SEL DN AN 6 9  
 L59 2 S E7-E12  
 L60 4 S L56,L59 AND L1-L59  
 L61 27 S L4 NOT L60  
 SEL DN AN 3 5 6 8 11  
 L62 5 S L61 AND E13-E27  
 L63 9 S L60,L62  
 L64 2257 S (CANCER? OR TUMOR? OR NEOPLAS?())SPECIFIC (L) ANTIGEN?  
 L65 5624 S (CANCER? OR TUMOR? OR NEOPLAS?())ASSOC? (L) ANTIGEN?  
 L66 2228 S L64,L65 AND L44-L46  
 L67 66 S L66 AND GLYCOSYLAT?  
 L68 4 S L67 AND DEGLYCOSYLAT?  
 L69 32 S L66 AND L9-L27  
 L70 125 S L29 AND L66  
 L71 27 S L66 AND L32  
 L72 9 S L71 AND L67,L69,L70  
 L73 1 S L69 AND L71  
 L74 4 S L69,L71 AND L67  
 L75 48 S L69,L71 NOT L67,L68,L72-L74  
 SEL DN AN 17 29 36  
 L76 3 S L75 AND E28-E36  
 L77 7 S L74,L76  
 L78 7 S L77 AND L1-L77

FILE 'HCAPLUS' ENTERED AT 14:43:45 ON 19 NOV 2002

FILE 'BIOSIS' ENTERED AT 14:44:06 ON 19 NOV 2002

E CALENOFF E/AU  
 L79 28 S E3,E4  
 E DITLOW C/AU  
 L80 21 S E3-E6  
 L81 45 S L79,L80  
 L82 34 S L81 AND (10064 OR 10054)/CC  
 L83 27 S L82 AND 345?/CC  
 L84 13 S 12504/CC AND L83  
 SEL DN AN 1 2  
 L85 2 S L84 AND E1-E4  
 L86 18 S L81 AND 00520/CC

FILE 'MEDLINE' ENTERED AT 14:50:14 ON 19 NOV 2002

E CALENOFF E/AU  
 L87 12 S E3,E4  
 E DITLOW C/AU  
 L88 9 S E3-E5  
 L89 20 S L87-L88  
 SEL DN AN 1 10  
 L90 2 S E1-E6 AND L89  
 L91 9728 S L64,L65  
 E PEPTIDE FRAGMENT/CT  
 E E4+ALL  
 L92 183 S L91 AND E4+NT  
 E REFERENCE VALUE/CT  
 E E4+ALL  
 L93 2 S E4+NT AND L92  
 E PREDICT/CT  
 E E 9+ALL  
 E PREDICT/CT  
 E E9+ALL  
 L94 13 S E81+NT AND L92  
 L95 151 S C4./CT AND L92



L96 13 S L93,L94 AND L95  
     E TUMOR CELLS/CT  
     E E4+ALL  
 L97 72 S E7+NT AND L92  
 L98 56 S E8+NT AND L92  
 L99 7 S L1./CT AND L92  
 L100 19 S L90,L93,L99,L96 AND L87-L99  
     E ANTIGENS, NEOPLAS/CT  
     E E4+ALL  
 L101 50974 S E8+NT  
 L102 183 S L91 AND PEPTIDE FRAGMENTS+NT/CT  
 L103 7 S L102 AND L1./CT  
     E ANTIGENS, SURFACE/CT  
     E E3+ALL  
 L104 219627 S E8+NT  
 L105 108 S L102 AND L104  
 L106 94 S L105 AND C4./CT  
 L107 40 S L105 AND TUMOR CELLS, CULTURED+NT/CT  
 L108 98 S L106,L107  
 L109 1 S L108 AND GLYCOSYLAT?  
 L110 1 S L108 AND DEGLYCOSYLAT?  
 L111 3 S L109,L110,L90  
 L112 2 S L111 NOT BOND/TI  
     SEL L103 4 6 DN AN  
 L113 2 S E1-E6  
 L114 4 S L112,L113 AND L87-L113  
 L115 98 S L108 AND D12./CT  
     E AMINO ACID MOTIF/CT  
     E E4+ALL  
 L116 4 S E36+NT AND L115  
     E MATH/CT  
     E E8+ALL  
     E STATISTIC/CT  
     E E2 9+ALL  
     E STATISTIC/CT  
     E E29+ALL  
 L117 991027 S E27+NT  
 L118 2105 S PEPTIDE FRAGMENTS+NT/CT AND L117  
 L119 52 S L118 AND L101  
 L120 6 S L7  
 L121 4 S L114 AND L87-L120

FILE 'MEDLINE' ENTERED AT 15:13:54 ON 19 NOV 2002

FILE 'WPIX' ENTERED AT 15:14:03 ON 19 NOV 2002

L122 22 S E3,E4  
     E DITLOW C/AU  
 L123 4 S E4  
 L124 24 S L122,L123  
 L125 1 S L124 AND (B04-C01? OR C04-C01?)/MC  
 L126 16 S L124 AND (B04-B04C? OR C04-B04C?)/MC  
 L127 1 S L124 AND (B04-K01? OR C04-K01?)/MC  
 L128 3 S L124 AND (B04-N02? OR C04-N02?)/MC  
 L129 1 S L124 AND (B14-H? OR C14-H? OR B12-G07 OR C12-G07)/MC  
 L130 2 S L124 AND P63?/M0,M1,M2,M3,M4,M5,M6  
 L131 2 S L129,L130  
 L132 1 S L131 NOT HELICOBACTER/TI  
 L133 1 S L132 AND L122-L132  
 L134 7 S (P63?/M0,M1,M2,M3,M4,M5,M6 OR (B14-H? OR C14-H? OR B12-G07 OR  
     SEL DN AN 2 3 5  
 L135 3 S E1-E6  
 L136 3 S L133,L135

L137

4 S L134 NOT L136

FILE 'WPIX' ENTERED AT 15:23:13 ON 19 NOV 2002